Remarks

Claims 1-12 were presented in the application as originally filed. Claims 1-12 were cancelled by preliminary amendment and replaced by claims 13-29; thus, claims 13-29 remain pending in the application.

Claim Rejections Under 35 USC §§ 102(b)

Claims 13-29 were rejected as being anticipated by **Larrson *et al.*, WO 96/02535** (Applicants' cited Reference BA).

As stated in response to the previous Office Action, Applicants do not dispute the Office's position that the reference teaches a method for the enantioselective production of the enantiomers of lansoprazole; in fact, Applicants specifically disclosed **Larsson** and incorporated its contents by reference into the present specification at page 6, last sentence, last paragraph. Significantly, however, a method for the stereoselective production of the individual enantiomers of lansoprazole is not the subject of Applicants' claims.

Applicants' invention is directed to various embodiments of methods of treating ulcers, gastroesophageal reflux disease, psoriasis, as well as various conditions caused by or contributed to by gastric hypersecretion. The claimed methods involve the administration of a therapeutically effective amount of optically pure *S*(-)lansoprazole.

While **Larsson** discloses a novel process for the enantioselective synthesis of single enantiomeric substituted sulphoxides which allegedly can be used in medicine and that the class of substituted 2-(2-pyridinylmethylsulphinyl)-1H-benzimidazoles is useful as inhibitors of gastric acid secretion (page 1, lines 20-22), Applicants maintain that **Larsson** does not anticipate the claimed invention.

"A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." Amgen, Inc. v. Hoechst Marion Roussel, Inc., 3314 F.3d 1313, 1354, 65 USPQ2d 1385, 1416 (Fed. Cir. 2003). In the present case, the disclosure in **Larsson** contains absolutely no discussion, comment, or teaching relative to the administration of a lansoprazole enantiomer to a patient, or in fact, specific disease states that would warrant such administration. Thus, the **Larsson** disclosure does not constitute an enabling disclosure sufficient for anticipation of the claimed invention and as such, the reference does not support a §102(b) rejection of the claims. Applicants, therefore, respectfully request that the rejection be withdrawn.

Claim Rejections Under 35 USC § 103

Claims 13-29 were rejected as being unpatentable over **Larsson** in view of Garnett (Applicants' cited Reference CB). It is the Office's position that since the **Larsson** reference teaches a method for the purification of the single lansoprazole enantiomers, and because the *racemic* lansoprazole compound is known to be effective as a gastric acid secretion inhibitor, it would have been obvious to one of skill to produce the single enantiomers and use one or the other in the treatment of ulcers and other digestive problems caused by excess gastric acid secretion.

Garnett teaches that the proton pump inhibitor, lansoprazole, like other PPIs including omeprazole, has the potential to significantly suppress the secretion of gastric acid and that it has been shown to be superior to standard dosages of H_2-antagonists in inhibiting gastric acid secretions and therefore, for treating acid-related disorders. **Garnett** further states that since neither lansoprazole nor omeprazole is clearly superior one to the other, the choice between lansoprazole and omeprazole will depend, in part, on cost (see page 1433, summary, last sentence.) On economic grounds, therefore, this statement seems to teach away from the desirability of producing an enantiomeric version of a pharmaceutical compound at increased production costs, when, like lansoprazole, the racemic version is well tolerated by patients and

has minimal adverse effects (page 1433, summary.) Hence, even in view of **Larsson's** disclosure of a process for enantioselective synthesis of lansoprazole, no motivation is provided by the teaching of **Garnett**.

Applicant would like to reiterate that as of Applicants' earliest disclosure date January 30, 1998 (filing date of US Provisional Application 60/073,141), lansoprazole was commercially available only as the 1:1 racemic mixture (PREVACID®, TAP Pharmaceuticals, Inc., Lake Forest, IL USA). In fact, PREVACID® remains the only commercially available lansoprazole product to date, and Applicants are not aware of any reports or disclosures that would indicate that any person of skill had been motivated by **Garnett** to synthesize one or both of the optically pure isomers of lansoprazole and test their therapeutic activity in the treatment of the various gastric conditions involved in Applicants' claims.

Secondly, as discussed in Applicant's earlier response, the reference: Arimori, K *et al.*, "Pharmacokinetic Differences Between Lansoprazole Enantiomers in Rats," *J. Pharm. Pharmacol.*, 50:1241-45 (1998; accepted for publication July 5, 1998), indicates that the state of the art subsequent to Applicants' priority date regarding the potential for differences in the pharmacological activities of the individual lansoprazole enantiomers remained uncertain.

Claims 26-29 are rejected as being unpatentable over **Larsson** et al in view of **Hasselkus**, US Patent 5,714,505.

Hasselkus teaches a method of treatment of psoriasis using omeprazole or lansoprazole. Like **Larsson** and **Garnett**, **Hasselkus** does not teach or fairly suggest that either of the enantiomers of lansoprazole would be particularly effective or more desirable than the racemate for use in the method. Thus, for reasons already stated above, there is no motivation to combine the teachings of **Hasselkus** with the teachings of **Larsson**.

The Office Action concludes with the statement that, as far as the Examiner is concerned, the **Larsson** reference represents an unclearable legal hurdle to patentability given disclosure of

its apparent synthesis and teaching of utility for S(-) lansoprazole. In Applicants' view, Larsson does not teach a utility for the (S) enantiomer of lansoprazole, rather, it only teaches a utility for racemic lansoprazole. In view of the art as a whole, therefore, it is unclear to Applicants how one of skill in the art would be motivated by the teachings of any of the cited references, either individually or in combination, to expend the time, effort and expense of producing an enantiomeric product when its benefit over the racemic compound has not been demonstrated.

Because the state of the art at the time of the invention was such that the person of skill would have believed that the two enantiomers provided nearly identical inhibitory activity, there would have been no motivation to undertake the time and expense to pursue the separation and purification of either enantiomer for its individual administration. This is clearly supported by the fact that lansoprazole remains commercially available only as a racemic mixture. Despite the lack of motivation to do so, in addition to the expenditure of time, resources and personnel required to pursue the separation, purification and testing of one or both of the lansoprazole enantiomers, Applicants have done just that, and have discovered significant advantages associated with the administration of the optically pure *S*(-)-enantiomer.

Withdrawal of the rejections under 35 USC § 103 is respectfully requested.

For the foregoing reasons, the claims are believed in condition for allowance and such action is respectfully requested. The dependent claims are believed allowable for the same reasons as the independent claims from which they ultimately depend, as well as for their additional limitations. Should the Examiner require clarification of any of the above, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

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